

- 1. A method for identifying inhibitor compounds capable of reducing the interaction between:
- 5 a) a first region which is a signature motif on a nuclear protein, and
  - b) a second region which is that part of a nuclear receptor which is capable of interacting with the nuclear protein through binding to the signature motif,

wherein:

the nuclear protein is a bridging factor that is responsible for the interaction between a

10 liganded nuclear receptor and a transcription initiation complex involved in regulation of gene expression;

the nuclear receptor is a transcription factor;

the signature motif is a short sequence of amino acid residues which is the key structural element of a nuclear protein which binds to a liganded nuclear receptor as part of the process

15 of the activation or repression of target genes; and in which the method comprises taking:

- i) the potential inhibitor compound;
- ii) the liganded nuclear receptor or a fragment thereof in which the fragment comprises the second region defined in this claim in b) above;
- 20 iii) a fragment comprising a signature motif of the nuclear protein; and
  - iv) detecting the presence or absence of inhibition of the interaction between ii) and iii).
  - A method according to claim 1 in which the signature motif is B<sup>1</sup>XXLL in which B<sup>1</sup> is any natural hydrophobic amino acid, L is leucine and X independently represents any natural amino acid.
- A method according to claim 2 in which B1 is leucine or valine.
  - 4 A method according to claim 3 in which B1 is leucine.
  - A method according to any one of claims 2-4 in which the signature motif is further defined as B<sup>2</sup>B<sup>1</sup>XXLL wherein B<sup>2</sup> is a hydrophobic amino acid.
- 6 A method according to claim 5 in which B<sup>2</sup> is selected from the group consisting of 30 isoleucine, leucine, methionine, phenylalanine, tryptophan, tyrosine and valine.





- 7. A method according to any one of claims 1-6 in which the nuclear protein is a coactivator.
- 8. A method according to claim 7 in which the coactivator is selected from the group consisting of RIP 140, SRC-1, TIF2, CBP, p300, TIF1, Trip1, Trip2, Trip3, Trip4, Trip5,
- 5 Trip8, Trip9, p/CIP, ARA70 & Trip230.
  - 9. A method according to any one of claims 1-6 in which the transcription factor is a steroid hormone receptor.
- 10. A method according to claim 9 in which the steroid hormone receptor is selected from the group consisting of oestrogen receptor, progesterone receptor, androgen receptor and 10 glucocorticoid receptor.
  - 11. A method according to claim 10 in which the steroid hormone receptor is oestrogen receptor.
  - 12. A method according to any preceding claim wherein the method is in the form of a 2-hybrid assay system.
- 15 13 A method according to any preceding claim wherein the potential inhibitor is in the form of a peptide library based on a signature motif as defined in any one of claims 2-6.
  - 14. A novel inhibitor identified according to the method defined in any one of claims 1-13 which reduces the interaction between
  - a) a first region which is a signature motif on a nuclear protein, and
- b) a second region which is that part of a nuclear receptor which is capable of interacting with the nuclear protein through binding to the signature motif, wherein:

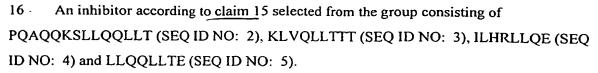
the nuclear protein is a bridging factor that is responsible for the interaction between a liganded nuclear receptor and the transcription initiation complex involved in regulation of

25 gene expression;

the nuclear receptor is a transcription factor;

the signature motif is a short sequence of amino acid residues which is the key structural element of a nuclear protein which binds to a liganded nuclear receptor as part of the process of the activation or repression of target genes.

30 15 An inhibitor according to claim 14 which is a peptide of less than 15 amino acid residues comprising the signature motif defined in any one of claims 1-6.



- An inhibitor according to claim 14 comprising an antibody which specifically binds to a signature motif on a nuclear protein.
  - A pharmacoutical composition which comprises an inhibitor as defined in any one of claims 14-17 or a pharmaceutically-acceptable salt thereof, in association with a pharmaceutically-acceptable diluent or carrier.
- 19 A method of mapping nuclear receptor interaction domains in nuclear proteins in
  10 which the method comprises analysis of the sequence of a nuclear protein for the presence of
  signature motifs as defined in any one of claims 1.6 in order to identify an interaction domain
  or a potential interaction domain.

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